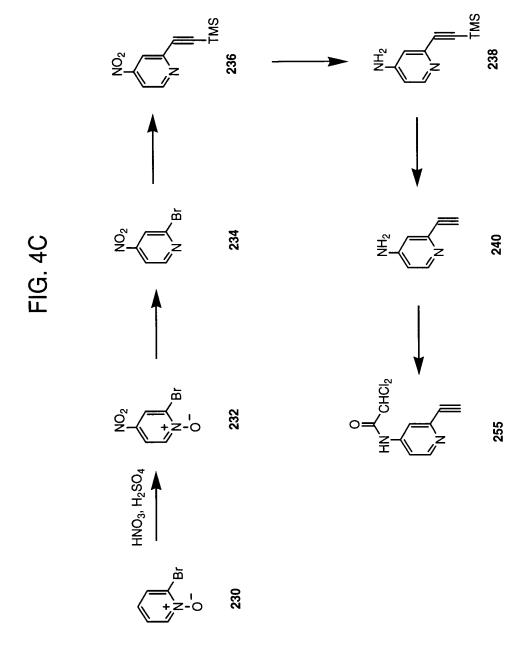
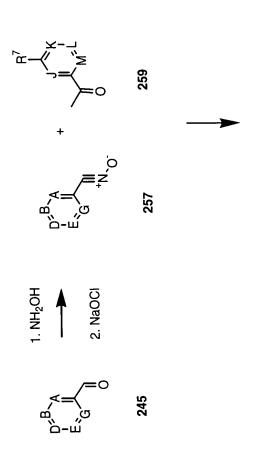
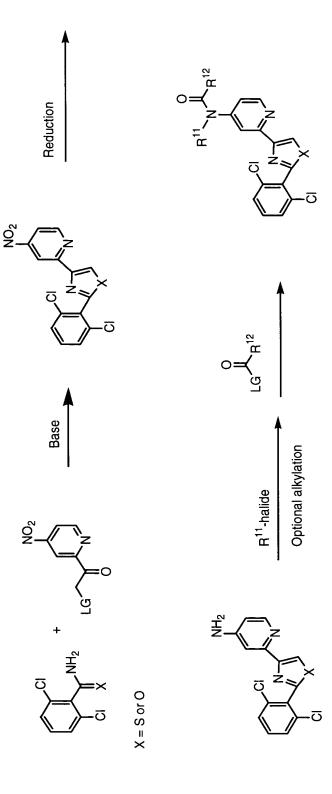
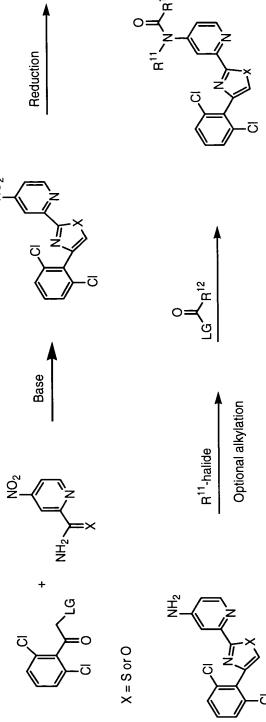
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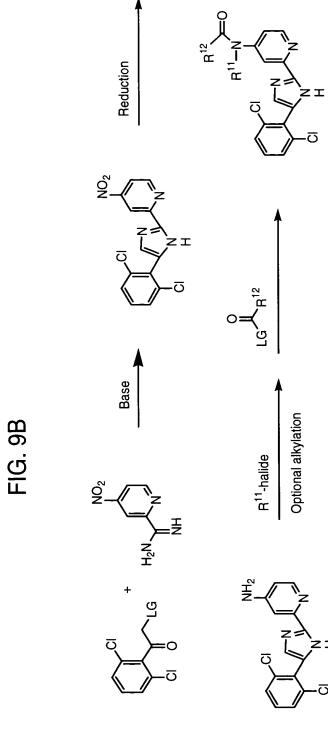
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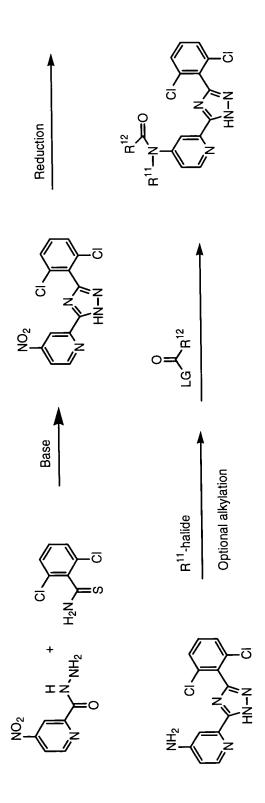


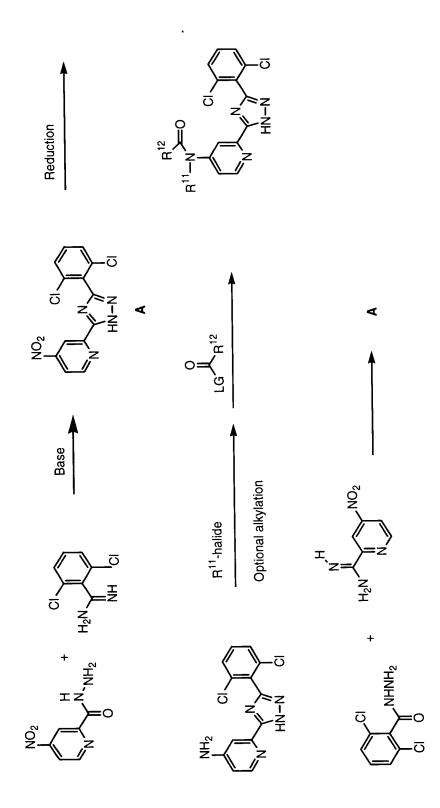








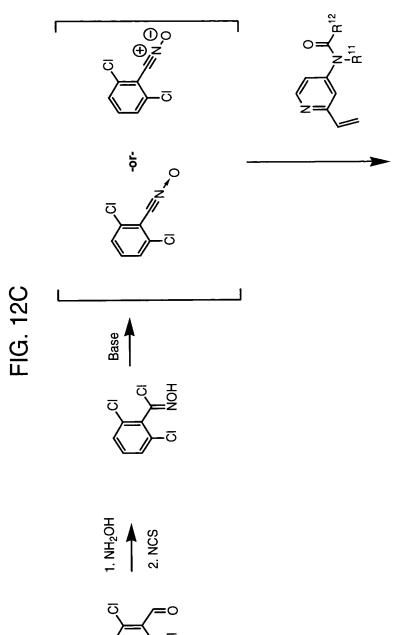


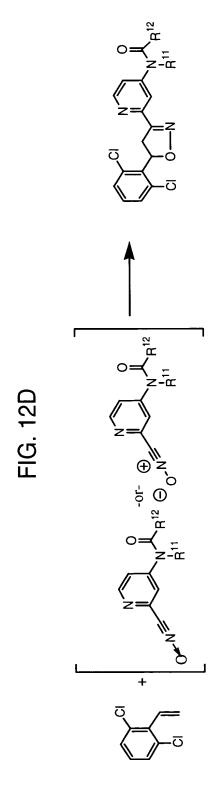


NH<sub>2</sub> Optional alkylation

R<sup>11</sup>-halide

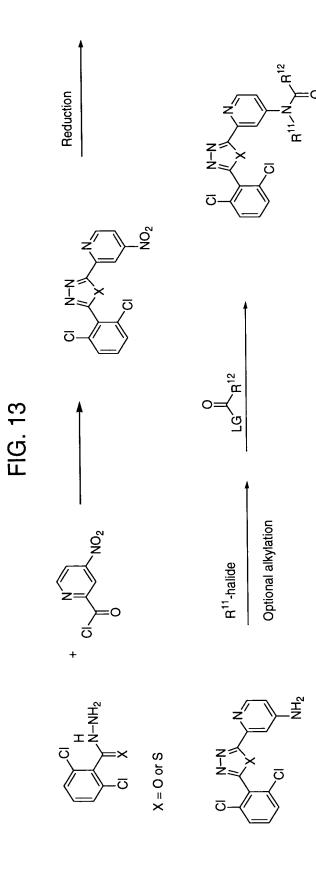
Reduction





or RX
$$X = leaving group$$

$$Y = leaving group$$



$$X = Br, 1$$

$$Y = Br, 2$$

$$Y = Br, 3$$

$$Y = Br, 1$$

$$Y = Br, 1$$

$$Y = Br, 2$$

$$Y = Br, 3$$

$$Y = Br, 4$$

$$Y = Br, 1$$

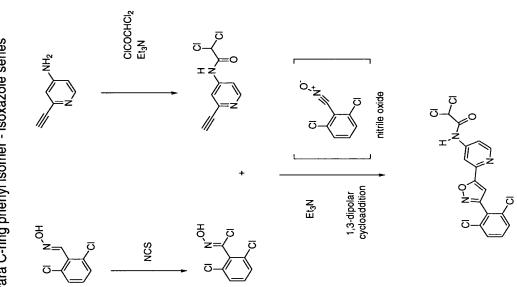
$$Y = Br, 2$$

$$Y = Br, 3$$

$$Y = Br, 4$$

$$Y =$$

Figure 16 Para C-ring phenyl isomer - isoxazole series

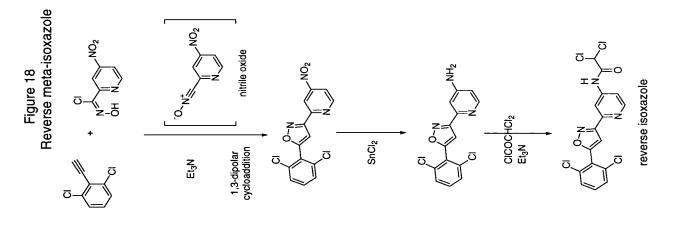


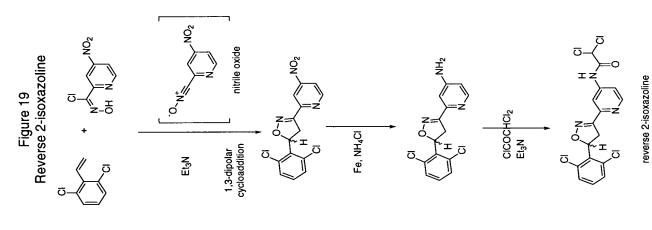
$$V=OH, CI \\ R_1=CI, Br, F, I \\ R_2=H, CI, Br, F, I$$

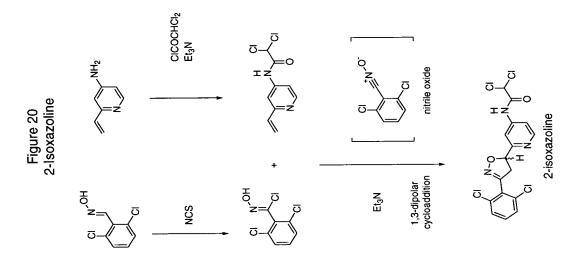
Method H

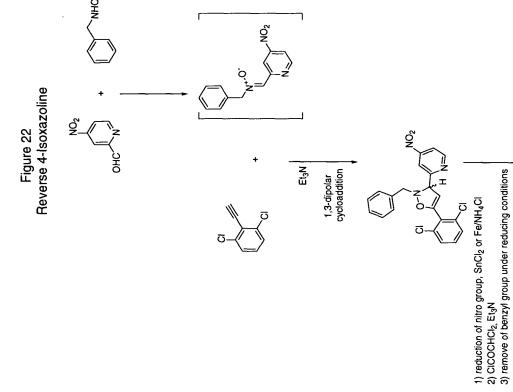
Figure 17

/









HPLC purifications

four diastereomeric isoxazolidines

four diastereomeric reverse isoxazolidines

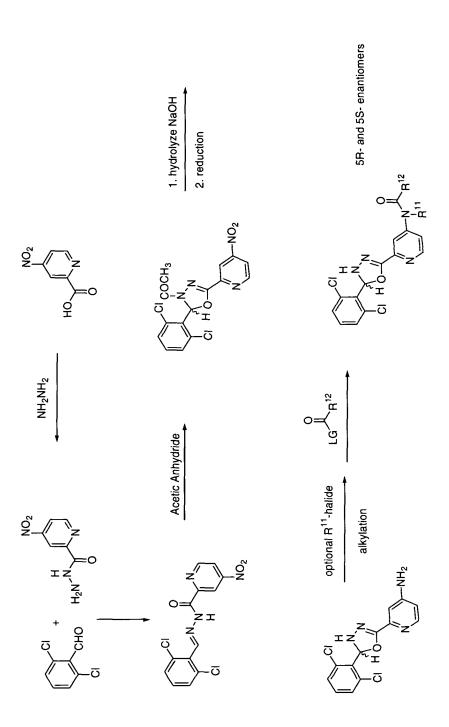
optional R<sup>11</sup>-halide

alkylation

cis- and trans- racemates 3R,5R-, 3S, 5S-, 3R, 5S-, 3S, 5R--diastereoisomers

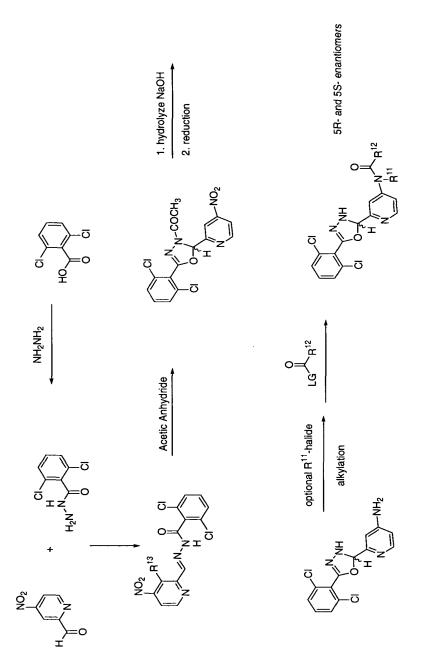
Bull. Chem. Soc. (Japan), 1989, 62, 3944-3949. Representative Reference:

Figure 28 4,5-dihydro-oxadiazoles



J.Chem.Research, Synopses, 1995, 88-89.

Figure 29 Reverse 4,5-dihydro-oxadiazoles



J.Chem.Research, Synopses, 1995, 88-89.

NH<sub>2</sub>NH<sub>2</sub>

<u>§</u>

optional R<sup>11</sup>-halide

alkylation

Representative Reference:

5R- and 5S- enantiomers

Oriental J.Chem, 2001,17, 513-514.

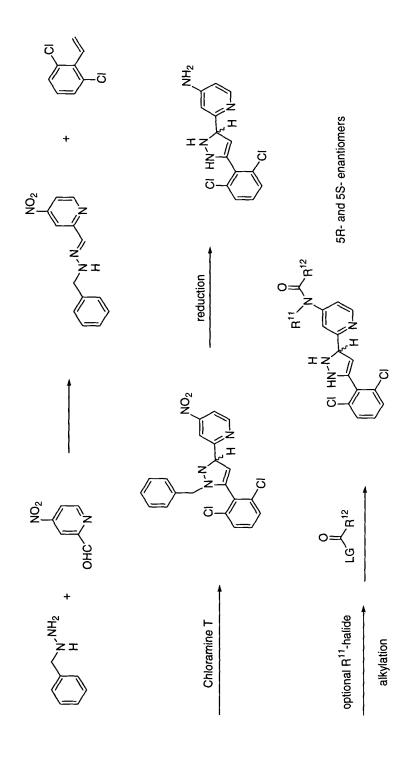
optional R<sup>11</sup>-halide

alkylation

Representative Reference:

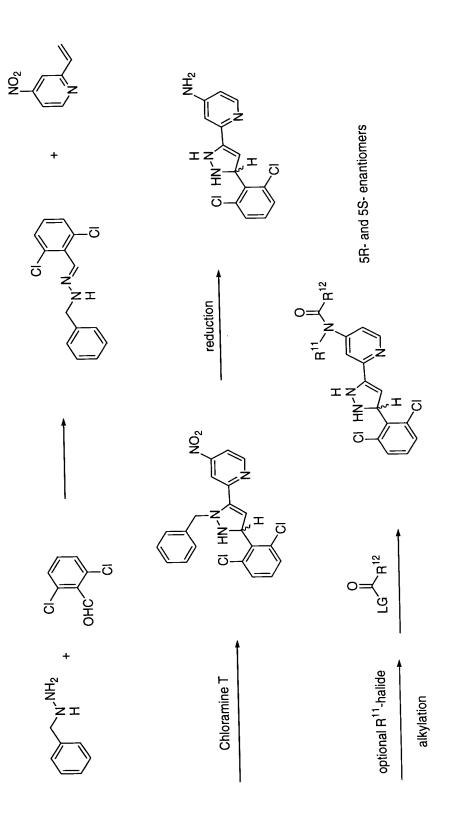
5R- and 5S- enantiomers

Oriental J.Chem, 2001,17, 513-514.

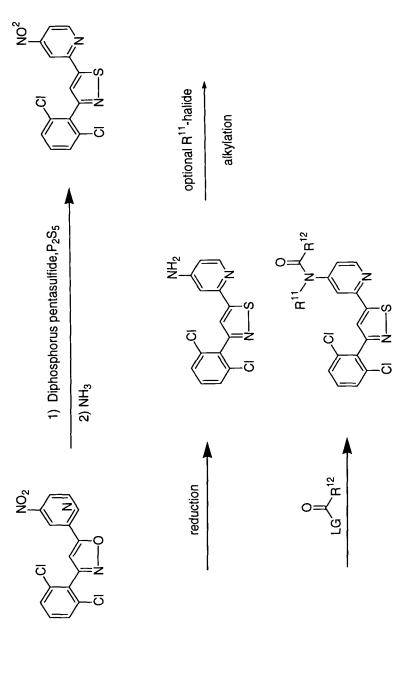


Synth. Commun., 1989,19, 2799-2807.

Figure 33 Reverse 3-pyrazolines

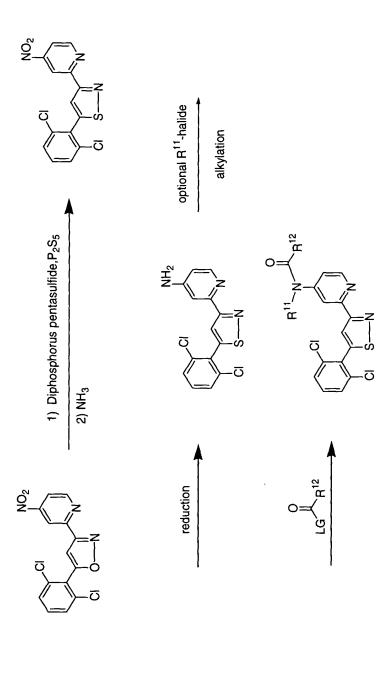


Synth. Commun., 1989,19, 2799-2807.

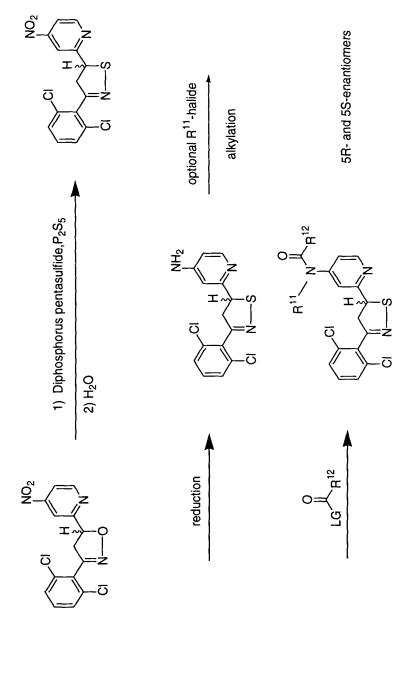


Tetrahedron, 1992,48, 8127-8142.

Figure 35 Reverse Isothiazole

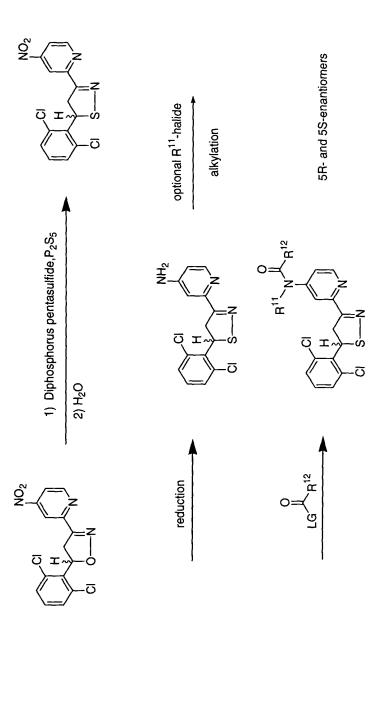


Tetrahedron, 1992,48, 8127-8142.



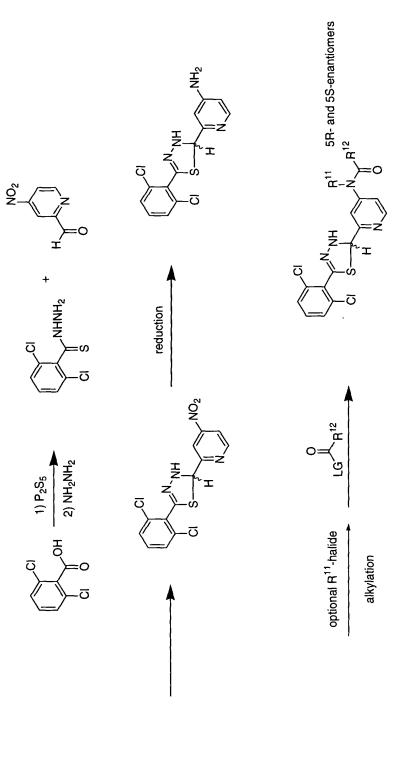
Asian J.Chem., 2000,12, 1358-1360.

Figure 37 Reverse 2-Isothiazoline



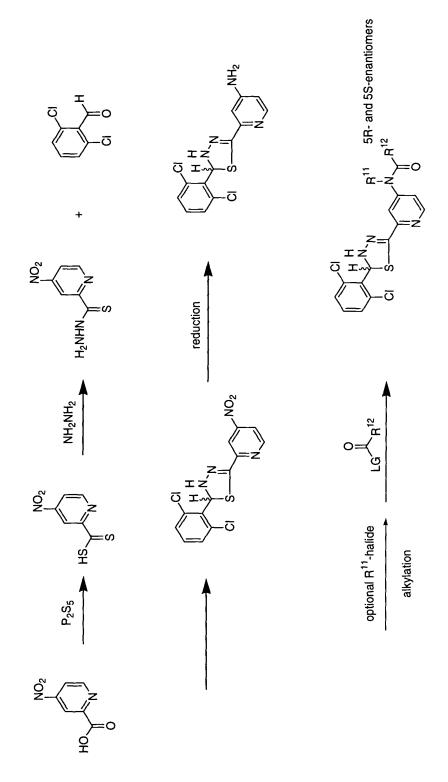
Asian J.Chem., 2000,12, 1358-1360.

Figure 38 4,5-Dihydro-1,3,4-thiadiazole



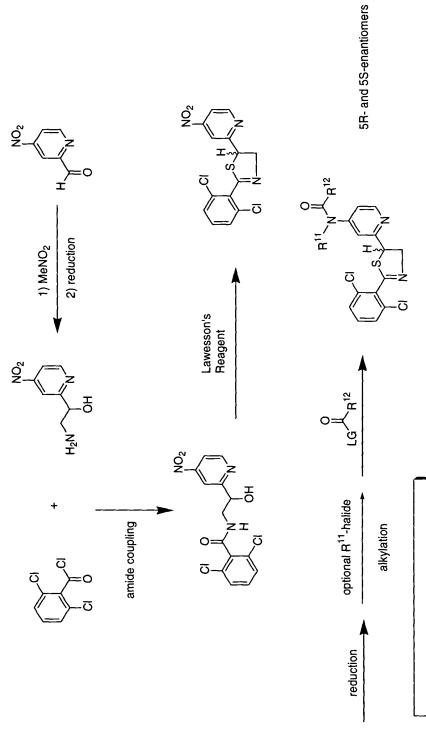
Sovrem, Aspekty Terorii i Prakt. Farmatsii, L., 1988, 90-96.

Figure 39 Reverse 4,5-Dihydro-1,3,4-thiadiazole



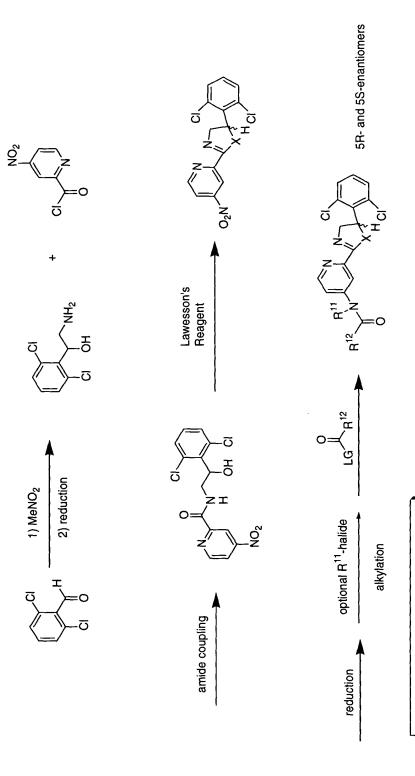
Sovrem, Aspekty Terorii i Prakt. Farmatsii, L., 1988, 90-96.

Figure 40 2-Thiazoline



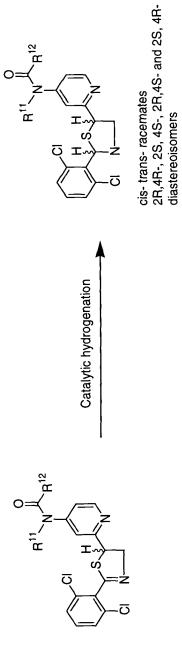
Collection of Czechoslovak Chemical Communications, 1978, 43(7), 1917-1923 J. Org. Chem., 1997, 62, 1106-1111.

Figure 41 Reverse 2-Thiazoline



Collection of Czechoslovak Chemical Communications, 1978, 43(7), 1917-1923 J. Org. Chem., 1997, 62, 1106-1111.

## Figure 42 Thiazolidines



Representative Reference:

See March's Advanced Organic Chemistry 5th Ed John Wiley & Sons, Inc. 2001, Topics related to catalytic hydrogenation.

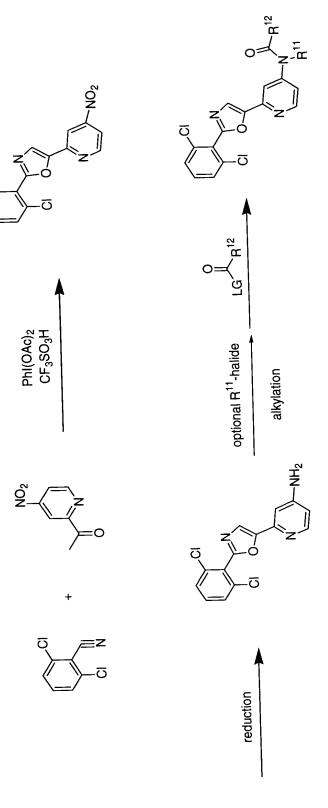
## Figure 43 Reverse Thiazolidines

cis- trans- racemates 2R,4R-, 2S, 4S-, 2R,4S- and2S, 4Rdiastereoisomers

Catalytic hydrogenation

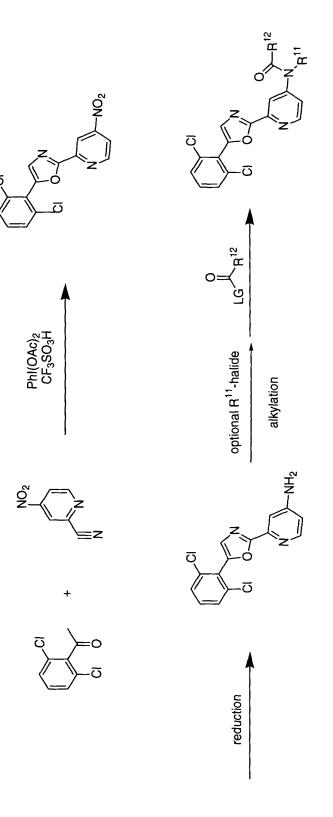
Representative Reference:

See March's Advanced Organic Chemistry 5th Ed John Wiley & Sons, Inc. 2001, Topics related to catalytic hydrogenation.

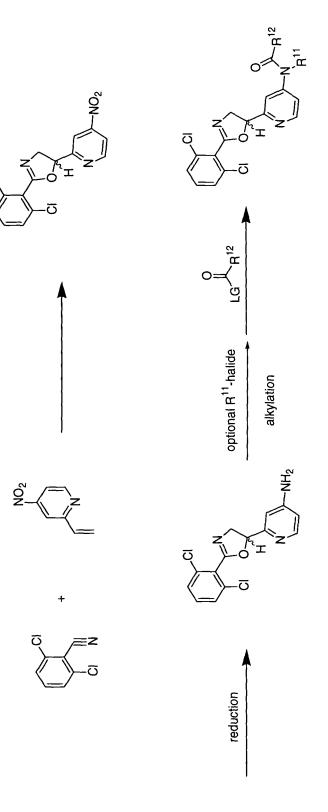


Varma, R.S et al J. of Heterocyclic Chem., 1998, 35(6), 1533-1534

Figure 45 Reverse Oxazole



Varma, R.S et al J. of Heterocyclic Chem., 1998, 35(6), 1533-1534



4R- and 4S- enantiomers

Representative Reference:

Li, Q et al Bioorg&Med. Chem.Lett., 2002, 12(3), 465-469.

5R- and 5S- enantiomers

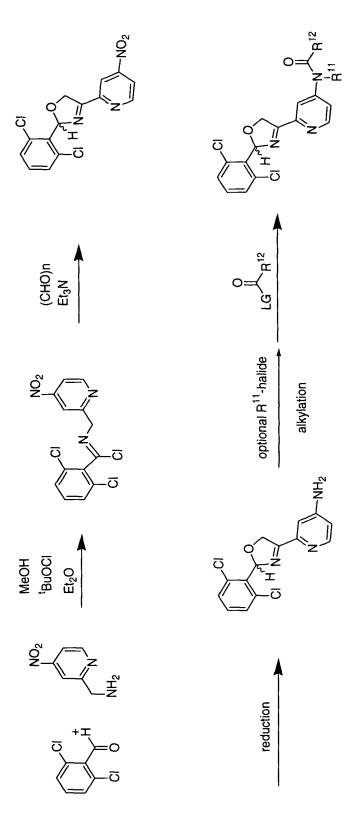
Representative Reference:

Li, Q et al Bioorg&Med. Chem.Lett., 2002, 12(3), 465-469.

2R- and 2S- enantiomers

Representative Reference:

Paul, H et al, Chem. Ber., 1965, 98, 1450 Huisgen, R et al, Angew. Chem., 1962, 74, 31.



2R- and 2S- enantiomers

Paul, H et al, Chem. Ber., 1965, 98, 1450 Huisgen, R et al, Angew. Chem., 1962, 74, 31.

Representative Reference:

optional R<sup>11</sup>-halide

reduction

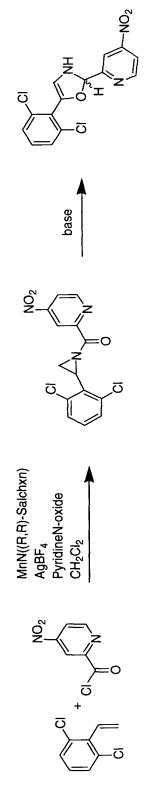
alkylation

2R- and 2S- enantiomers

Representative Reference:

Minakata, S et al., Tet Lett., 2001, 42(51), 9019-9022. Stamm, H et al., Chem. Ber., 1990, 123 (11), 2227-

2230.

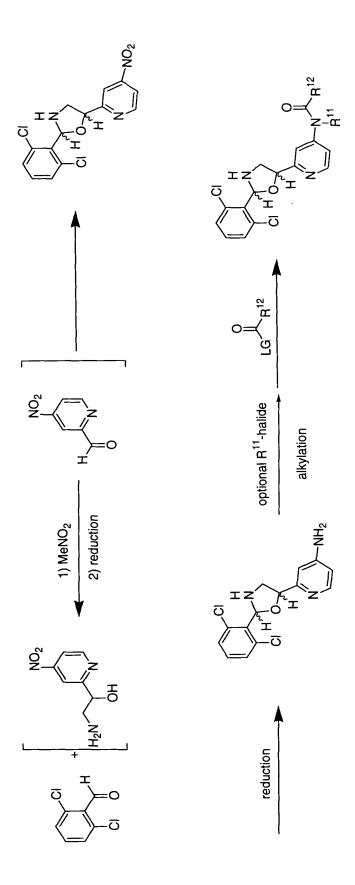


2R- and 2S- enantiomers

Representative Reference:

<u>Minakata, S et al., Tet Lett.,</u> 2001, 42(51), 90199022.

<u>Stamm, H et al., Chem. Ber.,</u> 1990, 123 (11), 22272230.

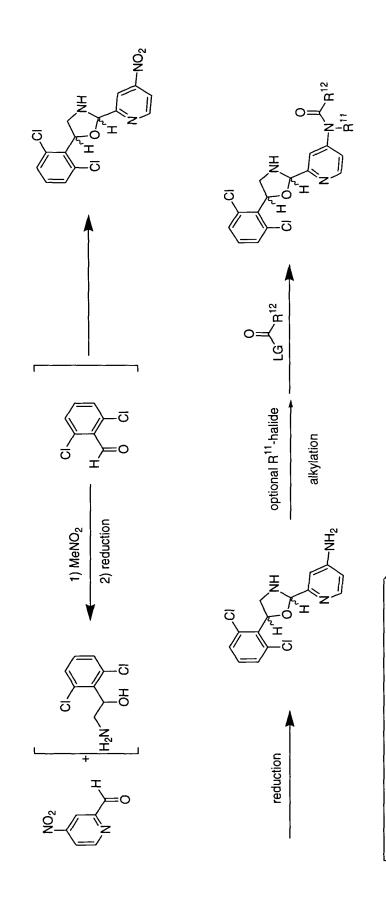


cis- and trans- racemates 2R,5R-, 2S,5S-, 2R,5S- and 2S,5R diastereoisomers

Schoenenberger, H et al., Archiv der Pharmazie 1975, 308(9), 717-719.

Representative Reference:

## Figure 53 Reverse Oxazolidines

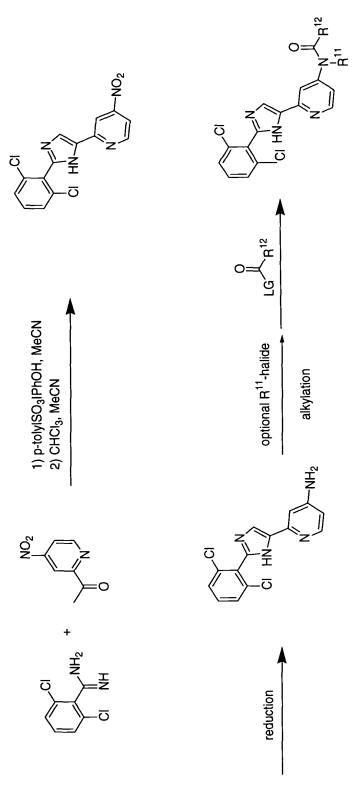


cis- and trans- racemates 2R,5R-, 2S,5S-, 2R,5S- and 2S,5R diastereoisomers

Schoenenberger, H et al., Archiv der Pharmazie 1975, 308(9), 717-719.

Representative Reference:

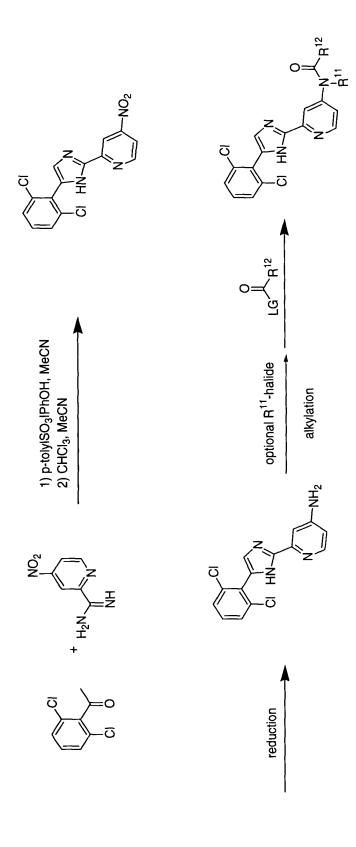




Representative Reference:

Zhang, P-F et al., Synthesis 2001, 14, 2075-2077

## Figure 55 Reverse Imidazole



Representative Reference:

<u>Zhang, P-F et al., Synthesis</u> 2001, 14, 2075-207

.

4R- and 4S- enantiomers

Representative Reference:

Molina, P et al., Synlett., 1995, 10, 1031-1032.

4R- and 4S- enantiomers

Molina, P et al., Synlett., 1995, 10, 1031-1032.

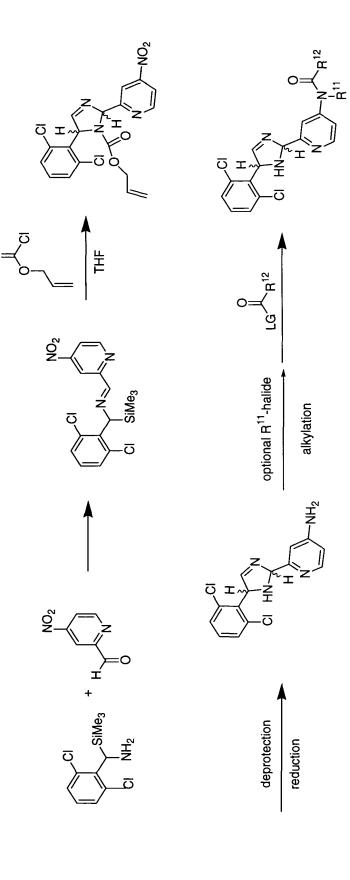
Representative Reference:

cis- and trans- racemates 2R,5R-, 2S,5S-, 2R,5S- and 2S,5R diastereoisomers

<u>Iyoda, M et al.,</u> Chem. Lett., 1995, 12, 1133-1134. <u>Katzenellenbogen, J.A et al.,</u> Tet. Lett., 1997, 38(25), 4359-4362.

Representative References:

## Figure 59 Reverse 3-Imidazolines



cis- and trans- racemates 2R,5R-, 2S,5S-, 2R,5S- and 2S,5R diastereoisomers

Representative References:

<u>lyoda, M et al.,</u> Chem. Lett.,1995, 12, 1133-1134. <u>Katzenellenbogen, J.A et al.,</u> Tet. Lett., 1997, 38(25), 4359-4362.

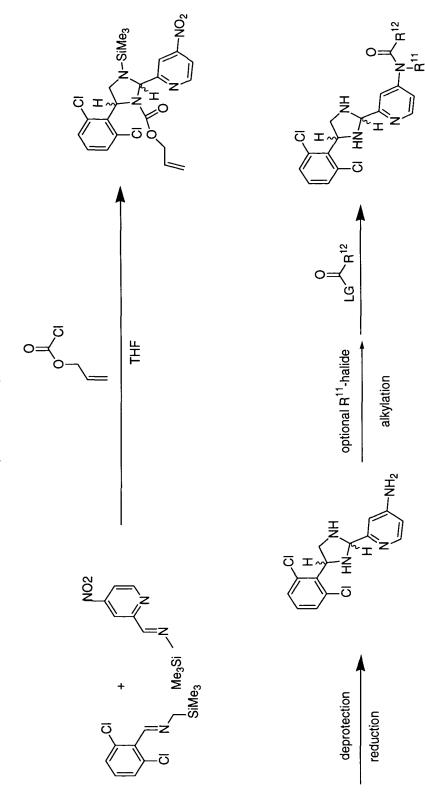


cis- and trans- racemates 2R,4R-, 2S,4S-, 2R,4S- and 2S,4R diastereoisomers

Representative References:

Achiwa, K et al Chem. Lett., 1981, 1213.

## Figure 61 Reverse Imidazolidines



cis- and trans- racemates 2R,4R-, 2S,4S-, 2R,4S- and 2S,4R diastereoisomers

Representative References:

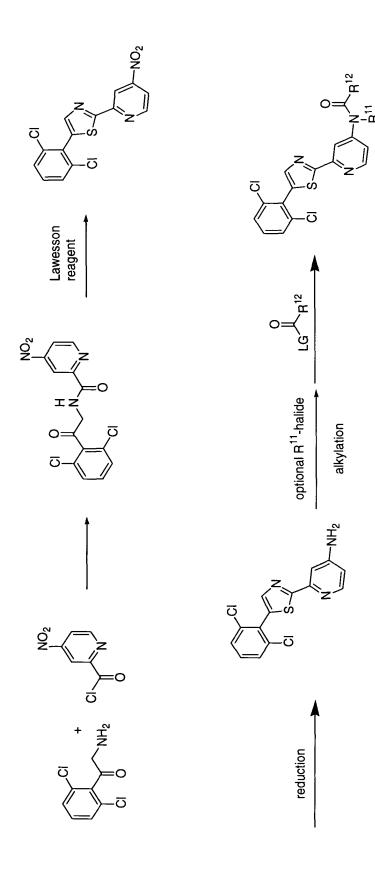
Achiwa, K et al Chem. Lett., 1981, 1213.

optional R<sup>11</sup>-halide alkylation reduction

Representative References:

Lhotak,P et al Collect Czech Chem., 1993, 58 (11 2720-2728.

Figure 63 Reverse thiazole



Representative References:

Lhotak, P et al Collect Czech Chem., 1993, 58 (11 2720-2728.